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9.403IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application	Edward L. Carver, Jr.	)	
of:	Steven J. Skiptunas	)	Group Art Unit: 1743
		)	
on:	APPARATUS AND	)	Examiner: L. Alexander
	METHOD FOR MIXING	)	
	FLUIDS FOR ANALYSIS	)	
		)	
Serial No.:	09/198,004	)	
		)	
Filed On:	November 23, 1998	)	(Docket No. 116310.0032)

Commissioner for Patents  
Alexandria, VA 22313

RESPONSE TO OFFICE ACTION

Dear Sir:

Applicant submits this Response to the outstanding Office Action received in connection with the above-identified application. Claims 1, 2-6, 31 and 33-47 are pending in this application. All claims stand rejected under 35 U.S.C. § 102(b) as being anticipated by EP 0107333 ("EP '333"), under 35 U.S.C. § 102(e) as being anticipated by Carver et al. (U.S. Patent No. 5,380,491), and under 35 U.S.C. § 102(b) as being anticipated by Yamamoto et al. (U.S. Patent No. 4,030,888). The Examiner's grounds for rejection are hereinafter traversed, and reconsideration is respectfully requested.

The Examiner states at page 2 of the Action that "Applicants' state the instant invention teaches mixing a plurality of reagent mixtures with a sample prior to analysis", and

further states, “With respect to the apparatus claims, these remarks are not convincing because the apparatus taught by EP 0107333 teaches a structure (e.g., multiple valves feeding into a single chamber for mixing) indistinguishable from that claimed.” (Office Action at page 2). It is respectfully submitted that the Examiner has not addressed Applicants’ remarks as set forth in the Appeal Brief and summarized below, and further, that the Examiner has ignored clear structural limitations of independent claims 1 and 42 as further summarized below. As set forth below, independent claims 1 and 42 include clear and unambiguous structural limitations that are drafted in “means-plus-function” language, that are not shown anywhere in the cited references. The Examiner asserts that EP ’333 “teaches a structure . . . indistinguishable from that claimed”, but fails to point out in any way the manner in which EP ’333 teaches the claimed structural limitations, much less on a clear limitation-by-limitation basis, as the Examiner is required to do. Further, it is respectfully submitted that the Examiner has failed to rebut the specific points raised below (and also in the Appeal Brief) addressing in detail the structural limitations of the independent apparatus claims, and the manner in which the each of the cited references fails to show each such limitation. It is important to note that in order to make a proper anticipation rejection, the cited reference must show every limitation recited in the claim. It is respectfully submitted that the Office Action fails to make a proper rejection under 35 U.S.C. §§ 102(b) or (e) with respect to each cited reference because it ignores clear and unambiguous limitations of the claims that are not shown anywhere in the cited prior art.

With respect to the method claims, the Office Action states at page 2 that “The method claims are directed to ‘pumping each of a plurality of reagent mixture components including

the sample of blood . . .’ The Office has read the claim as providing more than one stream, which includes the sample of blood. EP 0107333 meets this limitation by teaching the addition of a reagent mixture to the blood and the appropriate buffers, sheath fluids, etc.”. (Office Action at page 2). As with apparatus claims 1 and 42, and as summarized below, it is respectfully submitted that the Examiner has ignored clear and unambiguous limitations of independent method claim 31. As further summarized below, these claims limitations are not shown anywhere in each cited reference.

**A. EP ‘333, Carver et al. and Yamamoto et al. Do Not Teach The Invention Recited In Independent Claim 1.**

EP ‘333, Carver et al. and Yamamoto et al. each do not teach the combination of “means for combining at least one reagent-mixture component stream into at least one other reagent-mixture component stream for mixing the plurality of reagent-mixture components into a combined reagent-mixture stream” and “means for either chemically analyzing, or analyzing a particle distribution of, the selected reagent mixture in the combined reagent mixture stream”, as recited in claim 1.

Although EP ‘333 shows three blood sample-reagent mixtures and three sheath liquids (each of the three sheath liquids being optically compatible with a respective one of the blood sample-reagent mixtures), none of the blood sample-reagent mixtures is combined with any of the other blood sample-reagent mixtures. Further, although each of the blood sample-reagent mixtures is mixed with a respective one of the sheath liquids, they are not mixed until after they are each analyzed and upon exiting the flow cell. Applicants admit that EP ‘333 describes concomitant flow of a blood sample-reagent mixture and its respective sheath liquid

through the flow cell. However, contrary to the Examiner's assertion, this does not teach "means for combining ... for mixing ... into a combined ... stream", as recited in claim 1. Indeed, EP '333 explicitly teaches not to mix the concomitant flows prior to and within the flow cell. Moreover, EP '333 does not mix the concomitant flows until they exit the flow cell and are discarded as waste. Accordingly, EP '333 teaches away from the combination recited in independent claim 1.

More specifically, EP '333 teaches that reaction vessel 40 contains the blood sample and appropriate reagent mixture for counting and sizing red blood cells and platelets, reaction vessel 42 contains the blood sample and appropriate reagent mixture for counting and sizing basophils, and reaction vessel 44 contains the blood sample and appropriate reagent mixture for sizing and counting all other white blood cells except basophils. (See, e.g., page 10, line 29 through page 11, line 12 of EP '333). The sheath fluid reservoirs 96, 98 and 100 each contain a sheath liquid that is optically compatible with the respective mixture contained in a corresponding reaction vessel 40, 42 or 44. (See id.)

During operation, each sample-reagent mixture contained in a respective reaction vessel 40, 42, or 44 and the corresponding compatible sheath liquid contained in the respective sheath fluid reservoir 96, 98 or 100 are pumped through the flow cell 12. The sample-reagent mixtures contained in the reaction vessels 40, 42 and 44 are not pumped through the flow cell at the same time. Rather, only one sample-reagent mixture and corresponding sheath fluid are pumped through the flow cell at any one time. (See, e.g., page 4, lines 7-10, and lines 29-33 of EP '333).

EP '333 further teaches that a blood sample-reagent mixture and its respective sheath are selected for concomitant flow through the flow cell 12 (page 6, lines 25-28). However, the flow cell 12 does not combine the sample and sheath streams, as recited in independent claim 1. Indeed, EP '333 specifically teaches maintaining the sample and sheath fluid -- while being analyzed in the flow cell -- in two separate unmixed streams that are concentrically located at two different diameters. For example, EP '333 states: "the sheath stream flow cell 12 brings the sample and sheath streams introduced at inlets 26 and 28, respectively together to form a pair of concentric, substantially unmixed streams, with the sample stream at the center." (Page 7, lines 7-12 of EP '333, emphasis added). EP '333 further states: "This forms the concentric sample-sheath liquid streams through the flow cell under precisely controlled and coordinated, readily reproducible conditions of constant, and optimal, sample and sheath liquid stream diameters . . . ." (EP '333 at page 14, lines 4-7, emphasis added). Thus, the concentric sample-sheath liquid streams are not mixed prior to or during analysis in the flow cell, but rather are mixed only when discarded as waste in the flow cell outlet. Indeed, the very purpose of maintaining the separate, unmixed streams as taught by EP '333 is to facilitate analysis in the flow cell.

Thus, the clear and unambiguous teaching of EP '333 is to first premix the separate samples and reagents in the reaction vessels 40, 42 and 44, wherein each premixed sample-reagent mixture is defined by the respective test to be performed thereon. Then, to separately pump each reaction mixture through the flow cell 12 with its corresponding sheath fluid, and to maintain the reaction mixture and sheath fluid while being analyzed in the flow cell in two separate, unmixed streams that are concentrically located at different diameters. Accordingly,

EP '333 does not show in any way means for combining the separate reagent-mixture streams into a combined stream as recited in independent claim 1.

Yamamoto et al. show an automatic blood analyzer that is fixed to make the same dilution ratios, with the same volumes of reagent-mixture components for every blood sample. In addition, the fixed reagent mixtures are mixed in typical cuvette-type chambers, such as the chambers 6 and 11 of FIG. 1. Similarly, Carver et al. mix the blood sample with lysing agent A and/or lysing agent B in a typical mixing cuvette 13. In each reference, the samples and lysing agents are poured into and mixed in the cuvettes (not into a combined reagent-mixture stream), and then after they are mixed, they are poured out of, or pumped out of the cuvettes, and passed through a sensing cell for analysis. Thus, neither Yamamoto et al. nor Carver et al. teach means for combining one reagent-mixture component stream into another reagent-mixture component stream and forming a combined reagent-mixture component stream, as recited in independent claim 1. Rather, the reagent mixture components are poured into a cuvette, and mixed within the cuvette, not combined into a combined reagent-mixture stream, as recited in claim 1.

Accordingly, EP '333, Carver et al. and Yamamoto et al. each fails to teach the combination of “means for combining at least one reagent-mixture component stream into at least one other reagent-mixture component stream for mixing the plurality of reagent-mixture components into a combined reagent-mixture stream” and “means for either chemically analyzing, or analyzing a particle distribution of, the selected reagent mixture in the combined reagent mixture stream”, as recited in claim 1.

EP '333, Carver et al. and Yamamoto et al. also do not teach “means for forming each of a plurality of different selected reagent mixtures in the combined reagent-mixture stream by adjusting the flow rate of at least one of a plurality of reagent-mixture components in accordance with a flow-rate ratio of reagent-mixture components corresponding to each respective selected reagent mixture”, as further recited in independent claim 1. Rather, EP '333, Carver et al. and Yamamoto et al. each form different selected reagent mixtures by pre-mixing them in the reaction vessels or cuvettes. There is simply no teaching in any of the references of means for forming such mixtures by combining reagent-mixture streams, much less such means that adjust the flow rate of the components in accordance with a flow-rate ratio corresponding to the selected reagent-mixture ratio, as recited in claim 1.

Accordingly, it is respectfully submitted that EP '333, Carver et al. and Yamamoto et al. each wholly fails to teach the invention as recited in independent claim 1 for at least these reasons.

**B. EP '333, Carver et al. and Yamamoto et al. Do Not Teach The Invention Recited In Independent Claim 42.**

EP '333, Carver et al. and Yamamoto et al. do not teach the combination of “means for introducing at least one reagent-mixture component into a stream of at least one other reagent-mixture component to mix the plurality of reagent-mixture components into a combined reagent-mixture stream” and “means ... for at least one of (i) chemically analyzing and (ii) analyzing a particle distribution of the combined reagent-mixture stream”, as recited in claim 42.

As stated above, although EP '333 shows three blood sample-reagent mixtures and three sheath liquids (each of the three sheath liquids being optically compatible with a respective one of the blood sample-reagent mixtures), none of the blood sample-reagent mixtures is combined with any of the other blood sample-reagent mixtures. Further, the blood sample-reagent mixture and respective sheath liquid are maintained in separate, unmixed streams prior to and during analysis in the sheath stream flow cell, and are not mixed until after they exit the flow cell and are discarded as waste. Although EP '333 describes concomitant flow of a blood sample-reagent mixture and its respective sheath liquid, this does not in any way teach or suggest "means for introducing ... to mix ... into a combined ... stream", as recited in claim 42. Indeed, EP '333 explicitly teaches not to mix the concomitant flows, and therefore teaches away from the claimed invention. Thus, EP '333 cannot possibly teach or suggest the combination recited in independent claim 42.

Yamamoto et al. show an automatic blood analyzer that is fixed to make the same dilution ratios, with the same volumes of reagent-mixture components for every blood sample. In addition, the fixed reagent mixtures are mixed in typical cuvette-type chambers, such as the chambers 6 and 11 of FIG. 1. Similarly, Carver et al. mix the blood sample with lysing agent A and/or lysing agent B in a typical mixing cuvette 13. In each reference, after the samples and lysing agents are mixed in the cuvettes, they are then pumped through a sensing cell for analysis. Thus, neither Yamamoto et al. nor Carver et al. teach means for introducing at least one reagent-mixture component into a stream of at least one other reagent-mixture component and forming a combined reagent-mixture stream, as recited in independent claim 42. Rather, the reagent mixture components are poured into a cuvette, and

mixed within the cuvette, not combined into a combined reagent-mixture stream, as recited in claim 1.

In addition, none of the cited references teach an elongated mixing chamber including a first inlet port located at the upstream end of the mixing chamber, and a second inlet port located downstream of the first inlet port, wherein one of the first and second inlet axes is oriented at an acute angle relative to the other to introduce the respective reagent-mixture component stream into the mixing chamber in a different flow direction than the other reagent-mixture component stream to thereby create turbulence in the combined reagent-mixture stream, as further recited in independent claim 42. To the contrary, EP '333 teaches with reference to FIG. 1A conventional mixing cuvettes 40, 42 and 44 without any showing of first and second inlet ports, much less the specific configuration of inlet ports as claimed. The flow cell 12 shown in FIG. 1B of EP '333 is not a mixing chamber. Rather, as explained above, EP '333 specifically teaches away from mixing any fluids within the flow cell 12, and the flow cell 12 is constructed in a way specifically designed to prevent any such mixing from occurring. Similarly, Yamamoto et al. and Carver et al. teach conventional cuvettes or cuvette-type chambers, and do not show in any way the claimed mixing chamber, much less the specific configuration of inlet ports for intermixing the fluids and creating turbulence in the combined reagent-mixture stream, as claimed.

Accordingly, it is respectfully submitted that EP '333, Carver et al. and Yamamoto et al. each fails to teach the invention as recited in independent claim 42 for at least these reasons.

**C. EP ‘333, Carver et al. and Yamamoto et al. Do Not Teach The Invention Recited In Independent Claim 31.**

EP ‘333, Carver et al. and Yamamoto et al. do not teach “forming each of a plurality of different selected reagent mixtures in the combined reagent-mixture stream by adjusting the flow rate of at least one of a plurality of reagent-mixture components in accordance with a respective flow-rate ratio of reagent-mixture components forming each selected reagent mixture”, as recited in claim 31.

As stated above with respect to independent claim 1, EP ‘333, Carver et al. and Yamamoto et al. each form different selected reagent mixtures by pre-mixing them in the reaction vessels or cuvettes. There is no teaching or suggestion in any of these references of forming such mixtures by combining reagent-mixture streams, much less adjusting the flow rates of the components in accordance with a respective flow-rate ratio of reagent-mixture components forming each selected reagent mixture, as recited in independent claim 31.

Moreover, the Examiner’s statement at page 2 of the Action to the effect that EP ‘333 teaches “the addition of a reagent mixture to the blood” in no way addresses these clear limitations of the claim that are completely absent from each cited reference. Thus, EP ‘333, Carver et al. and Yamamoto et al. each cannot possibly teach the combination recited in independent claim 31.

It is therefore respectfully submitted that independent claims 1, 31 and 42 are not anticipated by EP ‘333, Carver et al. or Yamamoto et al. for at least these reasons. Because dependent claims 3-6, 33-41 and 43-47 each depend from one of these independent claims, it is respectfully submitted that these dependent claims are not anticipated by the cited

references for at least the same reasons as the independent claims, and for reciting additional patentable subject matter. Accordingly, all claims are believed to be allowable.

All issues raised by the Examiner having been addressed, an early action to that effect is earnestly solicited.

No fees in addition to those submitted herewith are believed to be required. However, if an additional extension of time is required, please consider this a petition therefor, and/or if additional fees are required, authorization is hereby given to charge our deposit account no. 50-1631.

If the Examiner wishes to discuss any of the issues addressed herein, or otherwise if it would facilitate the examination of this application, he is respectfully requested to call the undersigned at the telephone number below.

Respectfully submitted,

Date : August 27, 2003



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